Disclosing Conflicts of Interest to Research Subjects: an Ethical and Legal Analysis

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Abstract: In this article, I examine the ethical and legal issues related to disclosure of conflicts of interest to research subjects, and discuss some empirical studies related to the topic. I argue that researchers have an ethical obligation to disclose conflicts of interest to research subjects, provided that they take steps to help subjects understand information about conflicts of interest and how to interpret it. Researchers also may have a legal duty to disclose conflicts of interests to subjects, depending on the facts of the case and the court's interpretation of the law. To reinforce and clarify the legal obligation to disclose conflicts of interest, the federal regulations should be amended to include disclosure of conflicts of interest as one of the informed consent requirements. Institutional review boards play a key role in helping researchers to disclose conflicts of interests to subjects in an appropriate manner. Institutional review boards should approve the disclosure language in informed consent documents, and they should require researchers to disclose financial interests to research subjects, if they have any, as a condition of approval.

Key words: conflict of interest, biomedical research, ethics, informed consent, legal liability, institutional review boards, Jesse Gelsinger

Introduction:

The death of 18-year-old Jesse Gelsinger in a gene therapy experiment on September 17, 1999 provoked federal agencies, professional associations, academic institutions, and institutional review boards to reexamine policies relating to conflicts of interest (COIs) in biomedical research. Gelsinger had a genetic disease that caused his body to fail to produce sufficient quantities of ornithine transcarbamase, a vital live enzyme. Gelsinger lacked functional copies of the genes needed to make ornithine transcarbamase. Most people die from this disease in infancy, but Gelsinger was able to keep his condition under control with a special diet and drugs. Gelsinger agreed to participate in a study conducted by James Wilson and his colleagues at the University of Pennsylvania, because he hoped that the procedure would provide him with a cure for his illness. The goal of the experiment was to transfer functional copies of these liver enzyme genes to Gelsinger's liver. The experiment was classified as a Phase I study. Phase I studies are designed to test for the safety of new treatments but they are usually not expected to provide medical benefits to subjects. Gelsinger died because his body produced a massive immune reaction to the infusion of large quantities of an adenovirus into his liver, which was used as a vector for the liver enzyme genes (Marshall 2000, Krimsky 2003).

Following Gelsinger's death, the research community, the media, and the public soon learned about the individual and institutional financial interests at stake in this human experiment. The principal investigator, James Wilson, owned stock in Genovo, a company founded by him, which contributed $4 million per year to human gene therapy research at the University of Pennsylvania, where the experiment took place. Wilson also

held patents on gene therapy methods and techniques, and the University of Pennsylvania also owned stock in Genovo (Shamoo and Resnik 2003). Since 1999, the Department of Health and Human Services (DHHS), the Office of Human Research Protections (OHRP), the Food and Drug Administration (FDA), the Association of American Universities (AAU), and the Association of American Medical Colleges (AAMC) has issued reports, guidelines, and recommendations concerning COIs in research (Benbow 2003).

In a lawsuit filed against Wilson, the University of Pennsylvania, and other parties, Gelsinger's family claimed that Jesse Gelsinger did not receive adequate information about the risks of the experiment nor Wilson's nor the University of Pennsylvania's financial interests related to the experiment. Gelsinger was not provided with adequate information about the adverse effects in previous animal studies involving infusion of an adenovirus into the liver. Although Gelsinger was told that Wilson and the University could benefit financially from the experiment, he was not told about the specific nature of their financial interests, such as stock ownership. The lawsuit alleged that since Gelsinger did not receive this important information, he was not able to make an informed choice (Gelsinger Complaint 1999). If Gelsinger had known about these undisclosed risks and financial interests, according to the lawsuit, he would not have agreed to take part in the research study. He would not have wanted to take these risks or he would have been concerned that Wilson's and the University's financial interests could have undermined the integrity and safety of the research. Although the case was settled out of court, it highlighted the potential legal liability and the ethical hazards with not disclosing financial interests in research.

One of the most important issues relating to COIs in biomedical research is whether to disclose COIs to research subjects. This article will examine ethical and legal issues related to disclosing COIs to research subjects. It will argue that researchers have an ethical duty to disclose COIs to subjects, and that they may sometimes incur legal liability if they fail to adhere to this duty. Institutional Review Boards (IRBs) should play an important role in ensuring that researchers disclose COIs to subjects in an appropriate manner.

Defining Conflicts of Interest

Thompson (1993, p. 573) defines a COI for an individual as a situation in which that individual's "judgment regarding a primary interest (such as a patient's welfare or the validity of research) tends to be unduly influenced by a secondary interest, such as financial gain." As a result, the individual may fail to perform his or her primary ethical or legal obligations to research subjects, colleagues, research institutions, or the public (Thompson 1993; Shamoo and Resnik 2003). Some examples of financial interests that have been the subject of special concern include ownership of stock or equity, a leadership position, or a consulting agreement with a company sponsoring one's research; intellectual property rights, such as patents, related to one's research; and financial incentives, such as finder's fees or patient care costs, for enrolling subjects in clinical trials (Shimm and Spece 1991, Morin et al 2002; Krimsky 2003). Although COI rules and policies tend to focus on these types of financial interests, individuals may also have many other interests that can affect their judgment, including personal, professional, political, and intellectual interests. Many investigators have strong professional interests in enrolling subjects and completing clinical trials, even when they do not have any

financial interests directly related to the outcome, because they are interested in conducting and publishing research (Sollitto et al 2003).

Research institutions, such as universities, medical schools, or hospitals can also have COIs. A COI for a research institution is a situation in which the institution has a financial or other interest that tends to affect its decision-making. As a result, the institution may fail to fulfill its primary ethical or legal obligations to research subjects, the research profession, or the public (Resnik and Shamoo 2003). Research institutions, like individuals, have financial interests that could affect their decision-making, including ownership of stock or equity; partnerships and contracts with companies; and intellectual property rights (Moses and Martin 2001, Morin et al 2002).

COIs are an important ethical problem for scientific research for at least three reasons. First, COIs can bias the outcome of research. There is considerable evidence of a connection between the source of research funding and the outcomes of biomedical research studies (Krimsky 2003). Some studies have shown that 90% or more of publications sponsored by a pharmaceutical company favor that company's products (Friedberg 1999, Stelfox et al 1998). Pharmaceutical companies can use several tactics to achieve these results, including the suppression of research that yields negative results and biased interpretations for the data (Krimsky 2003).

Second, COIs can harm patients. Investigators with COIs may be tempted to "push the envelope" in research by bending or breaking ethical and legal rules for conducting research. As a result, subjects may be harmed. Gelsinger's death is a salient example of the risks associated with COIs. Because they did not tell Gelsinger about adverse effects in previous animal studies, researchers may have failed to adequately

inform Gelsinger of the risks of the gene therapy experiment. Furthermore, since Gelsinger did not have a significant chance of gaining a medical benefit from the experiment, the researchers may have enrolled him a study that did not have a justifiable risk/benefit ratio (Krimsky 2003).

Third, COIs can undermine the public's trust in the research enterprise, because research subjects, politicians and laypeople may view investigators with COIs as biased or unethical (DeAngelis 2000, Shamoo and Resnik 2003). Trust is a very fragile and precious commodity in biomedical research (Kass et al 1996). If people lose confidence in biomedicine, they will not enroll in clinical trials or provide financial support for research. Because trust is so important in research, researchers and research institutions need to address situations that only create the appearance of a COI, because the appearance of a COI can undermine trust, even if it does not affect judgment, behavior, or decision-making (Shamoo and Resnik 2003; Krimsky 2003).

Strategies for Dealing with Conflicts of Interest

There are three basic strategies for dealing with individual and institutional COIs: 1) disclosure; 2) conflict management; 3) prohibition (AAU 2001, AAMC 2002). The federal government requires disclosure of significant financial interests on federal grant applications (Public Health Service 1995). Most research institutions have policies requiring disclosure of COIs to supervisors, conflicts management committees, or institutional review boards (IRBs) (Cho et al 2001, Lo et al 2000, McCary et al 2001). Some journals also now have COI policies. Medical journals probably have a higher rate of COIs policies, since journals that adhere to the guidelines adopted by the International Committee of Medical Journal Editors (ICMJE) require disclosure of COIs (ICMJE

2003). A study conducted by Krimsky (2001) showed, however, that only 15% of 1,400 high impact journals have COI policies.

Disclosure embodies the virtues of transparency and openness, and allows concerned parties to use the information related to the COI to inform their own judgment and decision-making. Disclosure can also promote trust by relieving some of the suspicions that concerned parties may have, and by avoiding the inadvertent discovery of COIs. Nothing undermines trust more than finding out that a person or an institution did not disclose a COI that should have been disclosed. When this happens, concerned parties suspect that deception is afoot (Shamoo and Resnik 2003).

Sometimes the situation requires more than disclosure. Conflict management is the attempt to avoid or minimize the adverse effects of the conflict through plans and procedures. For example, suppose that a researcher is starting a new company that will sponsor his research. Assume also that he is the best person to conduct the research, and that it would not be advantageous for someone else to conduct the research at another university. A university COI committee might recommend that a group of scientists with no direct interest in the company and no personal relationships with the researcher oversee the conflict. The group could review the researcher's data, protocols, results, and publications for potential bias or other problems.

Some situations create such an enormous potential for bias or other adverse effects that the best strategy is to prohibit the conflict rather than to try to manage it. For example, suppose that a researcher is a member of an IRB that will be reviewing his research proposal. Although he can vote on other proposals on the agenda, he should leave the room and not vote on his own proposal, when the committee considers it. This

type of conflict has such a high potential for bias that it should be avoided whenever possible (Shamoo 1999).

How should one decide whether to disclose, manage, or prohibit a COI? The general rule is that the more problematic the COI, the more drastic the level of action required. Prohibiting a COI is more drastic than managing it, which is more drastic than disclosing it. Disclosure is almost always a useful strategy. To decide whether something more than disclosure is appropriate, one can consider two factors for assessing the COI (Resnik and Shamoo 2002):

- The probability that the COI will adversely affect judgment or decision-making (or the strength of the COI);
- The benefits/risks of the situation that creates the COI (or the utility of the COI).

Both of these factors need to be balanced in any assessment of a COI. A reasonable starting point for the development any a COI policy is to give these factors equal consideration. If the strength of the COI is high, and the utility of the COI is low, then the COI should be prohibited. For example, the IRB member's COI meets these conditions. If the strength of the COI is low, and the utility of the COI is high, then the COI should not be prohibited. For example, having one's research funded by a private company probably meets these conditions. Managing the COI may be the best strategy when the strength of the COI is medium and the utility is medium, the strength of the COI is high but the utility of the COI is high, or the strength and utility of the COI are both low. For example, in the situation where a researcher is starting a new company that will sponsor his research, the strength and the utility of the COI are both high, so managing the conflict may be the best solution.

Disclosing Conflicts of Interest to Research Subjects

Although there is near unanimous agreement that disclosure is a useful strategy for dealing with COIs, there is considerable disagreement about whether to disclose COIs to research subjects. The AAU (2001) recommends that financial conflicts of interest should be disclosed to the IRB, which can decide whether these should be disclosed to research subjects. Morin et al (2002) recommend disclosure of sources of funding and financial incentives to research subjects. The AAMC (2002) recommends that relevant conflicts of interest be disclosed to research subjects in a form determined by the IRB. The DHHS (2003) recommends that the IRB disclose sources of funding and payment arrangements to human subjects when that information is material to the informed consent process. Benbow (2003) recommends that IRBs should determine whether COIs should be disclosed to research subjects. Why is there agreement about disclosing COIs to supervisors, COI committees, IRBs, and journals, but a lack of agreement about disclosing COIs to research subjects? Why would it make any sense to tell all of these other parties about a COI but not tell the people participating in the research? To address this question, we shall consider the ethical arguments on both sides of the issue and then examine the legal aspects of the problem.

Autonomy

The first ethical argument for disclosing COIs to research subjects is that disclosure enhances autonomy and decision-making (Morin et al 2002; Krimsky 2003, Sollitto et al 2003). Information about the financial or other interests of researchers can play an important and decisive role in a subject's decision to participate (or not participate) in an experiment. To honor the subject's right to informed consent in

research, one must provide the subject with all relevant (or material) information, i.e. information that would have an affect on his or her decision-making process. Information about COIs can be relevant because a subject might decide not to enroll in an experiment, based on a financial disclosure. The Gelsingers argued, for example, that Jesse Gelsinger would not have decided to participate in the fatal experiment if he had had full knowledge of the financial interests of the investigator and the university. The reason why information about a COI could affect a subject's decision to enroll is that the information might give the subject a reason to believe that researcher's judgment could be affected by the COI (DHHS 2003).

Critics of disclosure claim that informing subjects about financial interests does not enhance autonomy and decision-making. According to this argument, disclosure of COIs can undermine autonomy by providing subjects with information that they do not understand or know how to interpret (Rodwin 1989, Thompson 1993, Barnes 2002; Miller and Horowitz 2000). A subject might overestimate the significance of a COI disclosure and regard it as a compelling reason not to enroll in a study, when, in fact, it would clearly be in the subject's best interests to enroll. Even if COI disclosures do not lead the subjects to make a poor decision, subjects may simply ignore the disclosures and treat them as just another part of the legalistic jargon that now takes up considerable space in the typical informed consent document. The best way to promote autonomy and informed decision-making is to provide subjects with a nominal amount of meaningful information, rather than with a flood of meaningless information.

Proponents of disclosure could respond to this criticism in two ways. First, the critique is nothing more than outdated paternalism. Many years ago, physicians made

similar arguments against informed consent in medicine. They argued that patients do not understand the information, that patients don't want to know the information, and that the information can be harmful to patients. Physicians, according to this argument, should decide what, when, and how much patients need to know (see Katz, 1984, for a discussion of this view). During the last thirty-five years, the trend in medical ethics has been away from paternalism and toward greater disclosure (Berg, Applebaum, Lidz, and Parker 2001). One might argue that research ethics has followed and should continue to follow a similar direction (Morin 1998). If subjects do not understand information relating to COIs, then researchers should explain it to them, instead of withholding it from them. IRBs can assist in this process by approving language on the informed consent document that subjects will be able to understand.

Second, the critique underestimates subjects' ability to understand and apply information about COI disclosures. An increasing number of professions, including law, real estate, banking, brokering, accounting, engineering, and journalism require that professionals disclose COIs to clients or other relevant parties. Most subjects can understand the principle that money can affect a person's judgment. Indeed, there is some evidence that subjects are more likely to understand COI information than they are likely to understand other information that is routinely disclosed in informed consent in research, such as complex experimental protocols, drug interactions, and medical risks (Kim et al 2004). People who are not familiar with the intricacies of biomedical research can still understand financial motivations and pressures.

Beneficence

The second argument for disclosing COIs to research subjects is that disclosure can benefit subjects. First, research subjects can derive positive benefits from their participation in decisions, such as improved education, satisfaction, and responsibility. When subjects have an opportunity to make decisions, they can view research as a partnership (Veatch 1987). Disclosure of COIs can play an important role in giving subjects a sense of partnership. Second, since research subjects can avoid some harms if they are given an opportunity to learn about COIs, disclosure of COIs can promote patient safety and welfare (Woodward 1999). For example, Jesse Gelsinger may have decided to not take part in the fatal gene therapy experiment if he had known specific facts about Wilson's and the University's financial interest. If he had decided not to take part in the experiment, he might still be alive today. If the research subject is not capable of making an informed choice, then his/her authorized representative, such as a parent or guardian, can make a choice that would protect the subject from harm. Third, disclosure may also promote subject safety by encouraging researchers to abandon or eschew potentially harmful practices. If a researcher knows that he (or she) must disclose a financial interest that could place that patient at risk, then he (or she) may decide to avoid the situation that creates that financial interest.

Critics of this argument claim that disclosing COIs often does not benefit patients and may do more harm than good. As noted earlier, subjects might overestimate the significance of a COI and not enroll in a research study that could offer them an important medical benefit. Additionally, COI disclosures may make subjects suspicious, confused, and or angry. They may also loose their trust in biomedical researchers and the

research enterprise. These significant harms would more than outweigh any good that could come from COI disclosures.

The proponent of COI disclosures could respond that this criticism is also an outdated type of paternalism. Critics of informed consent in medicine have argued that disclosing information to the patient can harm the patient in various ways. To avoid harming the patient, doctors should administer medical information in such a way that the benefits of disclosure outweigh the risks (see Katz, 1984, for a discussion of this view). Those who focus on the harms of disclosing COIs to research subjects are making the same sort of argument against disclosure. The arguments against paternalism in medicine hold equally well for paternalism in biomedical research. The patient (subject), not the doctor (or researcher) is generally the best judge of his or her own good. Almost all of the time, disclosing relevant information to the patient (or subject) will be more beneficial than harmful. Non-disclosure is justified only in very rare cases where disclosure could lead to imminent and severe harm to the patient (or subject) (Berg, Applebaum, Lidz, and Parker 2001).

Trust

One of the most influential arguments against disclosing COIs to research subjects is that disclosure will undermine the subject's trust in the researcher and in the research enterprise (Rodwin 1989). Subjects will become suspicious when they learn about the financial interests of investigators or research institutions. A subject may believe that the main reason why he or she is being asked to enroll in a human experiment is to make money for the researcher or the researcher's institution. Subjects may decide not to enroll if they find out about COIs. From this perspective, investigators

should not disclose COIs to prevent trust from being destroyed and to avoid undermining subject recruitment.

Proponents of disclosure can counter the trust argument by asserting that it is just another version of outdated paternalism. Physicians once employed the very same argument against disclosing information about risks to patients. They were afraid that if patients knew too much, they would lose the trust that is essential to the doctor-patient relationship, and they would not accept treatments that they needed (Katz 1984). Although patients at one time blindly put their trust in doctors, times have changed. Patients (and research subjects) now want information that they need to make decisions. Disclosure of information, including information about COIs, can help to build trust. There is even some evidence that COI disclosures do not have a significant adverse impact on subjects' willingness to enroll in research studies (Kim et al 2004). Indeed, one of the best ways to destroy trust is to not disclose a relevant financial (or other) interest to a subject when they are being recruited for a study, only to have the subject find out after the study is underway or has been completed. A patient (or subject) who learns about important information that was not disclosed is likely to feel betrayed or manipulated (Berg, Applebaum, Lidz, and Parker 2001).

To summarize, on balance, the ethical arguments favor disclosure of COIs to research subjects. Although there are some potential ethical problems with disclosing COIs to subjects, these problems can be overcome if researchers help subjects to understand information about COIs and how to interpret it. These obligations are no different from similar obligations researchers have in the informed consent process. Researchers should always strive to help subjects understand and interpret information,

whether it is information about benefits, risks, and alternatives, or information about COIs.

The Need for Additional Empirical Research

Additional empirical research on the effects of disclosing COIs to research subjects could help to resolve these ethical debates. It would be useful to have answers to the following questions:

1. Does disclosure of COIs to subjects improve or undermine subjects' decision-making?
2. Do research subjects want to know about COIs?
3. Does disclosure of COIs benefit or harm subjects?
4. Does disclosure of COIs build or destroy subjects' trust of researchers and the research enterprise?
5. Are subjects less likely to enroll in a research study if they learn about individual or institutional COIs than if they are kept ignorant of these relationships?

Although there is a substantial empirical literature on informed consent (see Sugarman et al 1999), very few studies examine the effects of disclosing COIs to subjects. However, one recent study by Kim et al (2004) sheds some light on questions 1, 2, 4, and 5. The study was an email survey of over 6000 potential research subjects drawn from the Harris Interactive Chronic Illness Database. Sixty four percent of the respondents to the survey replied that COI information was extremely or very important, and eighty seven percent believed that COIs should be disclosed as part of the informed consent process. More than half of the participants indicated that COI information would not affect their decision to participate in research, although a significant minority would be wary of

participation. The respondents were more concerned about individual COIs than institutional COIs. This study provides us with some information relevant to four of these questions, but it is only one study. Moreover, the study has some potential bias in that the research subjects were internet and computer users, who are probably more technologically and scientifically inclined than non-users. The subjects in this study may be the type of people who want and need more information than most people. Consequently, the study may overestimate the importance of COI disclosures to subjects. Clearly, there is a need for additional research in this area.

Legal Liability for Failure to Disclose Conflicts of Interest

Having addressed some of the ethical aspects of disclosing COIs to patients, I will now consider legal aspects of disclosure. For many researchers, IRBs and institutions, the argument that non-disclosure of COIs carries significant legal liability may have more weight than the argument that non-disclosure is unethical. As noted earlier, the Gelsinger complaint claimed that the investigators failed to fulfill their duty to fully disclose financial interests. To date, only two legal cases in the U.S. have addressed the issues of a researcher's legal duty to disclose financial interests to research subjects. Before examining these cases, it will be useful to review the legal basis for informed consent to human research in the U.S. There are at least two basic sources for a researcher's legal duty to obtain the informed consent of a research subject: 1) tort law, 2) federal research regulations (Morin 1998).

Failure to obtain informed consent from a research subject can result in tort liability if the subject is also a patient. Liability for failure to obtain informed consent may be based on three distinct torts: 1) battery; 2) negligence; 3) breach of fiduciary duty.

Liability for failure to obtain informed consent was originally construed as a tort known as battery, which is a harmful or offensive touching. The fact that the physician had obtained informed consent prior to touching the patient would be a legal defense to the tort of battery (Hall, Ellman, Strouse 1999). In the modern era, most physicians obtain some type of consent before touching patients, so battery is usually not an issue. However, a physician (or other professional) may obtain consent negligently. Thus, the modern tort of lack of informed consent is usually construed as a negligence claim (Hall, Ellman, and Strouse 1999). To prove negligence, the plaintiff must prove all six of the following elements: 1) the defendant had a duty to the plaintiff; 2) there was a standard of care for that duty; 3) the defendant breached the standard of care; 4) the breach caused harm to the plaintiff; 5) the harm was reasonably foreseeable; and 6) the plaintiff had some measurable injury (Diamond, Levine, and Madden 2000).

The standard of care for disclosing information is usually a key issue in informed consent litigation. Most of the jurisdictions in the United States follow the patient-centered "reasonable patient standard," which holds that the physician has a legal duty to disclose the information that a reasonable patient would want to know (*Canterbury v. Spence* 1972, *Cobbs v. Grant* 1972). Other jurisdictions still follow the "reasonable physician standard," which holds that the physician has a legal duty to disclose the information that a reasonable physician would disclose in the same or similar circumstances (Hall, Ellman, and Strouse 1999). Some jurisdictions, such as North Carolina, have adopted both standards (*Foard v. Jarman* 1990).

The tort of breach of fiduciary duty is based on the defendant's failure to honor his obligations to the plaintiff in a fiduciary relationship. 'Fiduciary' comes from the

Latin word 'fidelis,' which means faithful. The fiduciary has an obligation to act for the benefit of the fiducie (*Black's Law Dictionary* 1999). The law recognizes a number of different fiduciary relationships, including the physician-patient relationship (Richards and Rathbun 1993), the lawyer-client relationship (Rotunda 2001), and the relationship between the directors of a corporation and the corporation (Hamilton 2000).[1] The common feature of these different relationships is that the fiducie places considerable trust in the fiduciary, who assumes a certain amount of responsibility for the fiducie. Because this relationship exists, the fiduciary has an obligation to disclose information to the fiducie to protect the fiducie's interests. A crucial legal issue for a breach of fiduciary claim is whether a fiduciary relationship exists. Morin (1998) has argued that the relationship between the researcher and the research subject is a fiduciary one, but, as we shall see below, not all courts have adopted this view.

The federal research regulations constitute an entirely different source of the legal duty to obtain informed consent. Code of Federal Regulations, Title 45, Part 46, Subpart A (1991), otherwise known as "the common rule," has been adopted by 17 federal agencies, including the National Institutes of Health (NIH) and the National Science Foundation (NSF). The FDA adopted regulations that are very similar to the common rule, which are codified in Code of Federal Regulations, Title 21, Part 50 (1997). The federal regulations impose legal duties on researchers, research institutions, and IRB members. Someone who fails to adhere to the legal duties promulgated in the federal regulations may be liable for negligence as well as other torts (Resnik In Press; De Ville 2002). In *Grimes v. Kennedy Krieger* (2001), the defendants argued that they did not have a legal duty to the defendants, who were research subjects, on the grounds that the

research was not within the context of a therapeutic relationship. The researchers in *Grimes* were studying different lead abatement methods in houses where children were exposed to lead paint. The court rejected this argument and held that the researchers had legal duties to the subjects based on contractual obligations implied by the informed consent document as well as the federal research regulations. The *Grimes* court also held that the researchers had a legal duty to inform the parents of the subjects about the risks of lead exposure.

The federal regulations contain specific requirements for obtaining and documenting informed consent. The common rule requires researchers to inform subjects about the nature and purpose of the research; plans and procedures; any foreseeable risks of discomforts; benefits to the subject or others; alternatives procedures or treatments, if any; the extent to which confidentiality will be protected; and whom to contact for answers to questions or in the event of a research-related injury. The common rule also contains some additional requirements for consent, when appropriate, such as additional costs that the subject may incur or that significant new findings will be reported to the subject. It is important to note that none of these regulations specifically require researchers to disclose COIs to subjects.

Having reviewed some of the case law and regulations on informed consent in research, I shall examine two cases that have considered the issue of whether researchers have a legal duty to disclose COIs to research subjects. In *Moore v. Regents of the University of California* (1990), the plaintiff, John Moore, received treatment for a rare type of leukemia at the University of California, Los Angeles (UCLA), Medical Center. His physician, David Golde, recommended a splenectomy. After the operation, Golde

asked Moore to make several visits to the UCLA Medical Center to provide samples of skin, bone marrow, and sperm. The doctors told Moore that they needed these samples to monitor his health, but did not tell him that they needed the samples to develop a cell line from his tissue. Golde and other researchers were interested in Moore's tissue because it was overproducing valuable immune system proteins. The researchers signed an agreement with several pharmaceutical companies and the University of California to develop the cell line, which had an estimated market value of $3 billion (Resnik 2003). The researchers also obtained patents on the cell line.

When Moore discovered that his tissues were being developed for commercial purposes, he sued the researchers, the companies, and the university for several torts including conversion, breach of fiduciary duty, and lack of informed consent (*Moore* 1990). The court held that Moore could not sue for conversion because the cell line was the researchers' property, not his own. However, the court upheld Moore's claim for breach of fiduciary duty and lack of informed consent, because the physician-researchers did not tell him about their financial interests, which were material to Moore's consent. The information was material because a reasonable patient (subject) would want to know whether his physician has any economic or other interests that could affect his judgment. According to the court, "a physician must disclose personal interests unrelated to the patient's health, whether research or economic, that may affect the physician's professional judgment…failure to disclose such interests may give rise to a cause of action for performing medical procedures without informed consent or breach of fiduciary duty (*Moore* 1990 at 150)." In *Moore*, the court followed the reasonable patient

standard in holding that the physician has a responsibility to disclose information about COIs, and that a reasonable patient would want to know that information.

Thus, *Moore* supports a legal duty for physician-researchers to disclose COIs to subjects when those COIs may affect their judgment. It is also worth noting that several cases involving managed care contracts also support the physician's duty to disclose financial or other interests to his patient if these interests could affect his judgment. (See *Arata v. Avedon* 1993, *DAB v. Brown* 1997 and *Neade v. Portes* 1999).

In *Greenberg v. Miami Children's Hospital* (2003), the plaintiffs were human tissue donors and a private foundation that helped Reuban Matalon, a physician, develop a genetic test for Canavan disease. Matalon and the Miami Children's Hospital patented and commercialized the test without telling or obtaining permission from the tissue donors or the foundation about their plans. The plaintiffs sued Matalon and the hospital for lack of informed consent, breach of fiduciary duty, conversion, unjust enrichment, and several other torts. The plaintiffs argued that Matalon had breached his fiduciary duty to the donors and his duty to obtain informed consent, and they cited *Moore* to support their argument. However, the Florida court did not follow *Moore* on the grounds that there was no therapeutic relationship between the plaintiffs and Matalon, since Matalon was collecting tissue samples but not providing medical treatment. The court also held that it would not impose a duty to disclose financial interests on researchers in this case because this could impose an unworkable mandate on researchers and could have a chilling effect on research (*Greenberg v. Miami Children's Hospital* 2003 at 1070). In holding that researchers do not have a fiduciary duty to subjects when conducting non-therapeutic research, the court in *Greenberg* declined to follow *Grimes v.*

Kennedy Krieger Institute (2001), which held that researchers have fiduciary duties to subjects in non-therapeutic research.

In *Greenberg*, the plaintiffs also argued that the federal research regulations impose a duty of informed consent on researchers. The court admitted that that these regulations impose a duty of informed consent on research, but it held that this duty did not include a duty to disclose financial interests (*Greenberg v. Miami Children's Hospital* 2003 at 1069). As noted earlier, the federal research regulations do not specifically require that researchers disclose COIs to subjects. The requirement that comes closest to imposing a duty to disclose financial interests is the requirement to disclose any foreseeable risks, since a COI could constitute a risk to the research subject if it affects the researcher's judgment (Sollitto et al 2003). The court in *Greenberg* also declined to impose a fiduciary duty on the researchers, which would have implied a duty to disclose financial interests, on the grounds that the relationship between the plaintiffs and Matalon was not based on an acceptance of trust. According to the court, the plaintiffs donated their tissues to Matalon but did not make the assumption that he would protect their interests.

It is also worth noting that the court dismissed the plaintiffs' conversion claim on the grounds that they did not have a property interest in their donated tissue. ("Conversion" is a claim for wrongful possession or disposition of someone else's property.) The court followed *Moore* on this point (*Greenberg v. Miami Children's Hospital* 2003 at 1076). However, the court did not dismiss the plaintiffs unjust enrichment claim, because the plaintiffs had shown that 1) they conferred a benefit on the defendant; 2) the defendant knew about this benefit; 3) the defendant accepted the

benefit; and 4) it would be inequitable for the defendant to keep the benefit without paying for it (*Greenberg v. Miami Children's Hospital* 2003 at 1073).

In my opinion, I think the court in *Greenberg* erred when it said that researchers in a non-therapeutic relationship with subjects do not have fiduciary duties to subjects, because research subjects place a great deal of trust in researchers, even when they do not expect to benefit medically from research. Subjects trust researchers to disclose relevant information, to safeguard their safety, to minimize risks, and to protect privacy and confidentiality. The relationship is not like a relationship between two contracting parties; it is more like a partnership (Veatch 1987). In the law, partners have fiduciary duties toward one another (Hamilton 2000).

However, I agree with the court that the federal regulations do not mention or even imply a duty to disclose COIs. We have no evidence that the drafters of the regulations ever intended to include disclosure of COIs as a requirement for researchers. To remedy this situation and to clarify the scope of the legal duty to disclose COIs, the federal regulations should be amended so that they require researchers to disclose COIs to research subjects (Sollitto 2003).

In sum, whether a researcher would incur legal liability for failing to disclose financial interests to subjects depends on the facts of the case as well as the court's interpretation of informed consent law. If the researcher has a therapeutic relationship with his subjects, then he will probably have a duty to disclose financial or other interests that could affect his judgment. If he does not have such a relationship, then he may not have such a duty, depending on how the court views the case. If the court follows *Grimes*, then it would probably impose a duty to disclose financial interests on all

researchers. If it follows *Greenberg*, it may only impose the duty on researchers who have a therapeutic relationship with their subjects. In any case, state and federal law remains unsettled in this area, since only a couple of state courts have considered these questions.

Conclusion

In this article I have examined the ethical and legal issues concerning disclosure of COIs to research subjects. The arguments in favor of disclosure are: 1) disclosure promotes autonomy; 2) disclosure benefits subjects; 3) disclosure builds trust. The arguments against disclosure are: 1) disclosure does not promote autonomy; 2) disclosure may harm subjects; 3) disclosure undermines trust. Although additional empirical research is needed to help inform these ethical issues, on balance, the ethical arguments favor disclosure, provided that it is handled appropriately. Researchers should do more than just disclose information about COIs to subjects; they should also help subjects to understand and interpret this information.

I have also argued that researchers may have a legal duty to disclose COIs to subjects, depending on the facts of the case and the court's interpretation of the law. Two sources of law provide a legal basis for a duty to disclose COIs: 1) tort law; 2) the federal research regulations. Malpractice law most clearly supports a duty to disclose COIs when the researchers have a therapeutic relationship with their subjects. Although the federal regulations impose a legal duty to obtain informed consent from subjects on researchers, they do not specifically state or imply a duty to disclose COIs to subjects. To strengthen and clarify the legal obligation to disclose COIs, the federal regulations

should be amended so that disclosure of COIs is one of the informed consent requirements (Sollitto et al 2003).

I also propose that IRBs can and should play a key role in helping researchers address these issues in their research proposals and in approving appropriate language in informed consent documents. My analysis agrees with AAMC's (2002) recommendation that COIs should be disclosed to research subjects in a form determined by the IRB, but it also disagrees with AAU's (2001) recommendation that the IRB can determine whether COIs should be disclosed to research subjects. The main problem with allowing the IRB to determine whether COIs should be disclosed is that this leaves too much discretion to individual IRBs, and opens the door to inconsistency and unfairness. Some IRBs might take a strong stance in favor of disclosure, while others might not. As a result, research subjects would be treated differently under different IRBs. Allowing this much discretion would also encourage researchers to "shop" for IRBs that do not require disclosure of COIs. Another problem with allowing the IRB to determine whether COIs should be disclosed is that individual IRB members may have an interest in not requiring disclosure, since the may have their own financial interests related to research. To avoid these problems, there should be one standard for all IRBs: no approval of human research proposals unless researchers with COIs plan to disclose these interests to research subjects during the informed consent process. IRBs may determine how to interpret and apply this standard, but it should be the same standard for all IRBs.[2]

Notes

[1] There is large body of legal scholarship on many different types of fiduciary duties, which I do not intend to explore in this paper. For an introduction to fiduciary duties in human subjects research, see Benbow (2003).

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